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Via Email and Federal Express

National Vaccine Program Office
Office of the Assistant Secretary for Health
Department of Health and Human Services
Hubert H. Humphrey Building
200 Independence Ave, SW -- Room 725H
Washington, DC 20201-0004

Dear Sir or Madam:

Introduction.

I am submitting the following preliminary comments regarding the "PANDEMIC INFLUENZA PREPAREDNESS AND RESPONSE PLAN," Department of Health and Human Services ("DHHS"), Draft, August 2004 (the "Draft Pandemic Preparedness Plan") (http://www.hhs.gov/ nvpo/pandemics/execsumm8.12.doc. http://www.hhs.gov/nvpo/ pandemicplan/index.html). If there is a later opportunity to modify these comments or submit additional comments, or if these comments must be submitted in a different format, please let me know.

A. The Present State of a Possible Pandemic.

From published reports (M., "Enhanced: Public Health Risk from the Avian H5Nl Influenza Epidemic," *Science* 14 May 2004; 304: 968-969; "Experts Probe Flu Death, Call for Poultry Vaccination," *Science* 1 October 2004; 306: 31), avian influenza now appears to be somewhere between pandemic phases 0.2 and 0.3 (as that terminology is used in the Draft Pandemic Preparedness Plan, Executive Summary, p. 5). Accordingly, preparedness for a possible avian influenza pandemic should be a national - and international - priority.

B. General Comments Regarding Annex 5: "Vaccine Development and Production."

The *New York Times* recently reported that Chiron was also one of only two U.S. companies working on developing a vaccine for avian influenza A(H5Nl). (See "Experts Confront Hurdles in Containing Bird Flu," September 30, 2004.) Whether the recent

developments regarding Chiron's production of other influenza vaccines will adversely affect its work on an avian influenza vaccine remains to be seen.

Furthermore, that article also reported that "[0]ther drug makers have given several reasons for not making vaccines," including (a) "that intellectual property rights on new techniques used to make the vaccine remain unsettled" and (b) the worry that "they could be exposed to considerable liability if they put out a new vaccine without lengthy safety tests first." I am very concerned that these legal issues - in addition to numerous scientific and financial issues - are impeding the rapid development and manufacture of vaccines for avian influenza in large volumes. (If avian influenza becomes truly virulent, one suspects that demand for such a vaccine in the United States, and throughout the world, could make the current controversies over failures to produce sufficient quantities of other influenza vaccines appear almost inconsequential.)

I have not seen where such legal issues are specifically addressed in the Draft Pandemic Preparedness Plan. For example, while Appendix 5 does recommend an action to, "[p]rovide incentives for new vaccine manufacturers to enter the U.S. market to increase production capacity and, through diversification, enhance the probability that vaccine will be produced rapidly and made available early," p. 9, this is not the same as removing legal disincentives for new vaccine manufacturers to enter that market. While Appendix 5 also refers to $150 million in RFPs between FY'04 and FY 'OS, p. 8, it does not demonstrate that those RFPs will be sufficient to overcome the legal concerns identified in the *New York Times* article.

C. Specific Preliminary Questions Regarding Annex 5: "Vaccine Development and Production."

While considerable work appears to have gone into the Draft Pandemic Preparedness Plan, I believe there are additional questions that it should address, particularly with regard to Annex 5. Although the limited number of influenza vaccine manufacturers licensed for the U.S. market is noted in the Executive Summary, at p. 9, my questions focus on the overall issues of whether the plan could and should do more to ensure that there will be a sufficient number of developers and manufacturers capable of producing a vaccine, in a timely manner, to avert a true pandemic.

My specific questions are:

1. Has adequate information been obtained?

Has the DHHS obtained sufficient information from potential developers and manufacturers of avian influenza vaccines (including private companies, universities, other research institutions, and other non-profit organizations, both within and outside the United States) to know (a) whether there are additional such organizations that would

consider developing or manufacturing such a vaccine for the U.S. market, and (b) ifso, what concerns are keeping them from doing so?

What information has the DHHS obtained in this regard?

What surveys have been conducted?

What are the concerns of such potential additional developers and manufacturers?

Does the Draft Pandemic Preparedness Plan address all of those concerns? If not, how will such additional concerns be addressed in new actions to improve vaccine development and production?

If all such information has not been obtained, should it be obtained? If so, how will it be obtained, by when, and how will it be made available for further public comment?

2. What metrics will be used?

The Draft Pandemic Preparedness Plan discusses several actions "to improve vaccine development and production" (Appendix 5, pp. 6f.), but what metrics will be used to assess the effectiveness of such actions?

How will responsible persons - and the public - know whether these actions are successful or not?

What metrics will be used to assess whether timely progress is being made to increase the number of potential developers and manufacturers of avian influenza vaccines?

How many doses of an avian influenza vaccine should be stockpiled to protect the entire U.S. market?

What are reasonable numbers of (a) developers and (b) manufacturers to ensure the timely delivery - even in the face of periodic manufacturing difficulties - of a sufficient number of doses of an avian influenza vaccine to protect the entire U.S. market?

How will success be established?

How will possible failure be noted? How will possible failure be noted sufficiently quickly to allow time for pursuing other courses of action before a pandemic arises?

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3. What specific timetables will be followed?

Again, with regard to the actions "to improve vaccine development and production" (Appendix 5, pp. 6f.), what specific timetables will be followed?

How will responsible persons - and the public - know whether the contemplated actions are being carried out in a timely manner?

How long will it take to improve development and production sufficiently to have available at least 30 million doses of an avian influenza vaccine? (Best, worst, and likely cases?)

How long will it take to improve development and production sufficiently to have available at least 300 million doses of an avian influenza vaccine? (Best, worst, and likely cases?)

How long will it take to improve development and production sufficiently to have available at least I billion doses of an avian influenza vaccine? (Best, worst, and likely cases?)

4. Who will be held accountable?

Again, with regard to the actions "to improve vaccine development and production" (Appendix 5, pp. 6f.), who will be held accountable for ensuring that these, or other actions, are successful?

Which individuals are directly and personally responsible for these matters? How will their performance be monitored and reviewed?

Who supervises such persons? How will the actions of those supervisors be monitored and reviewed? Who will monitor and review their supervisory work?

5. How will Congress and the public be kept informed?

By what means will the responsible persons and their supervisors make known the status of all actions "to improve vaccine development and production" (Appendix 5, pp. 6f.) to Congress and the public?

Are periodic reports contemplated? If so, how frequently will they be made, and what information will they provide? How will such reports be distributed?

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6. Is funding adequate?

Is the funding described in the Draft Pandemic Preparedness Plan truly adequate to support all necessary actions "to improve vaccine development and production"? (Appendix 5, pp. 6f.)

How would the timetable for developing and manufacturing at least 30 million doses of an avian influenza vaccine be affected if funding were increased by 300% in the current fiscal year? By 1OOO%?

How would the timetable for developing and manufacturing at least 300 million doses of an avian influenza vaccine be affected if funding were increased by 300% in the current fiscal year? By 1OOO%?

How would the timetable for developing and manufacturing at least 1 billion doses of an avian influenza vaccine be affected if funding were increased by 300% in the current fiscal year? By 1OOO%?

Would a prize or guaranteed contract for a certain number of doses have a material effect on increasing the speed of developing and manufacturing an avian influenza vaccine? If so, how large must a prize be to have a significant material effect? If so, how many doses must be included as part of such a guaranteed contract?

7. Are actual or perceived legislative or regulatory obstacles preventing other developers and manufacturers from entering the market?

Have actual or perceived legislative or regulatory obstacles been addressed with possible new developers or manufacturers?

If so, what obstacles have been identified? How could any such obstacles be overcome?

If not, why have such issues not been addressed?

How long is it likely to take to obtain regulatory approval for the release of experimental versions of avian influenza vaccines? What could be done to shorten the time for obtaining such regulatory approval? In a true pandemic emergency, what authority exists for expediting regulatory approval in the United States?

8. Have the legal concerns identified in the *New York Times* article been addressed?

Is it true "that intellectual property rights on new techniques used to make the vaccine remain unsettled"? If so, what are those specific issues, and how could they best be

addressed? What specific patents or other intellectual property rights are at issue, and who controls the rights to those patents or other rights?

Is it true that potential developers or manufacturers of an avian influenza vaccine worry that "they could be exposed to considerable liability ifthey put out a new vaccine without lengthy safety tests first"? If so, what could be done, specifically, to overcome such concerns?

How could existing legislation concerning indemnification for vaccine production and distribution be modified (a) to address such concerns, if any, and (b) to ensure that experimental avian influenza vaccines are covered?

9. How are efforts being coordinated internationally?

How are efforts to increase the number of potential developers and manufacturers of avian influenza vaccines being coordinated internationally?

What could be done to enhance international cooperation in this regard?

10. How can others help?

How can individuals and groups outside the DHHS support the DHHS and help improve the Draft Pandemic Preparedness Plan? How can we help prepare for a possible pandemic?

Conclusion.

The Draft Pandemic Preparedness Plan is an extremely important step towards addressing what may become a problem of global proportions. At the present time, no one knows whether, or how quickly, avian influenza may transform itself into an extremely virulent disease. Current mortality rates for the disease are extremely worrisome. How mortality rates would be affected in the event of an actual pandemic - when health care resources could be stretched to the breaking point - is not known. What we do know is that avian influenza could, even in a very short time, become extremely dangerous.

It is my sincere hope that these comments may be of use in strengthening the Draft Pandemic Preparedness Plan. We should all work to prepare as well as we can for a possible pandemic. Thank you for taking the time to consider these questions. If I can provide you with any additional information, or if there are other means by which I can stimulate further dialogue concerning these issues, please let me know. Any responses from you would be most appreciated.

Sincerely yours,

John Kelley